

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: 28-JUN-2012

Subject: **Fludioxonil.** Registration # 64864-AT ecoFOG-80 FDL on Pome Fruit. **Review of New Formulation.**

PC Code: 071503

Decision No.: 456487

Petition No.: NA

Risk Assessment Type: NA

TXR No.: NA

MRID No.: 48630609

DP Barcode: D396217

Registration No.: 64864-AT

Regulatory Action: Section 3 Registration

Case No.: 7017

CAS No.: 131341-86-1

40 CFR: §180.516

REVIEWER: George F. Kramer, Ph.D., Senior Chemist
Risk Assessment Branch 1 (RAB1)
Health Effects Division (HED, 7509P)

THROUGH: David E. Hrady, Acting Branch Chief
RAB1/HED (7509P)

TO: Erin Malone/Shaja Joyner, RM 20
Registration Division (RD, 7505P)

Fludioxonil, 4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile, is a contact fungicide, which inhibits protein kinase, leading to reduced fungal growth and development. Tolerances are currently established for residues of fludioxonil in/on various plant commodities at levels ranging from 0.01-500 ppm [40 CFR §180.516], including the pome fruit crop group (5.0 ppm). Scholar™ 50 WP (EPA Registration #100-969), a wettable powder (WP) consisting of 50% fludioxonil, is currently registered for postharvest use on pome fruit. Pace International is proposing to register ecoFOG-80 FDL, an 8% liquid formulation intended for thermal electrofogger use on pome fruit.

CONCLUSIONS/RECOMMENDATIONS

As the submitted residue data are adequate to demonstrate that the proposed thermal electrofogger use will not result in residues that exceed the established tolerance of 5.0 ppm for pome fruit, HED recommends in favor of the proposed registration of ecoFOG-80 FDL.

DETAILED CONSIDERATIONS

Proposed Use: The currently registered use of Scholar™ 50 WP on stone fruit are summarized in Table 1.

Table 1. Currently Registered Postharvest Uses for Scholar™ 50 WP.				
Crop	Application Type	Rate	# Applications	Comments
Pome Fruit	High-Volume Spray	0.25 to 0.5 lb ai in 25-100 gallons of water	2	To treat 200,000 lbs of fruit (total of 0.16 oz ai per ton of fruit).
	Low-Volume Spray	0.25 to 0.5 lb ai in 7-25 gallons of water	2	
	Dip	0.25 to 0.5 lb ai in 100 gallons of water	2	Dip for ~30 sec.

Pace International is proposing to register ecoFOG-80 FDL, an 8% liquid formulation intended for thermal electrofogger use on pome fruit (summarized in Table 2).

Table 2. Proposed Postharvest Uses for ecoFOG-80 FDL.				
Crop	Application Type	Rate	# Applications	Comments
Pome Fruit	Thermal electrofogger	0.17 oz ai to treat 1 ton of fruit	1	Do not apply to fruit previously treated with fludioxonil via drench or dip/wash.

Residue Data: Pace has submitted residue data reflecting the proposed thermal electrofogger use on pome fruit (MRID# 48630609.der.doc):

A single post-harvest trial using apples was conducted during 2011. EXC6021 (liquid end-use product; 8% fludioxonil) was applied post-harvest by thermal fogging to Red Delicious apples in a simulated controlled-atmosphere cold storage warehouse at a nominal rate of 0.0094 lb ai/ton. The untreated fruit samples were taken one day prior to application. Four treated samples were sampled at a 1-day post-treatment interval (PTI). Samples were stored frozen from collection to analysis for <1 month, an interval supported by available storage stability data.



Samples were extracted and the extract was analyzed by gas chromatography with a mass-selective detector (GC/MSD) for residues of fludioxonil. The method was adequately validated in conjunction with the analysis of treated samples and limit of quantitation (LOQ) was 0.1 ppm. Residues of fludioxonil in the control samples were <LOQ. A single application of fludioxonil (EXC 6021) resulted in maximum fludioxonil residues of 0.26-0.34 ppm (n=4) with a mean of 0.303 ± 0.038 ppm in apples sampled at a 1-day PTI (Table 3).

TABLE 3. Summary of Residue Data from Post-harvest Apple Trials with Fludioxonil.									
Commodity	Method of Applic.	Total Applic. Rate (oz ai/ton)	Pyrimethanil Residue Levels (ppm)						
			n	Min.	Max.	HAFT ¹	Median	Mean	Std. Dev.
Apple, fruit	Postharvest thermofog	0.15	4	0.260	0.340	NA ¹	0.306	0.303	0.038

¹ HAFT = highest-average field trial. NA = not applicable to this submission.

Conclusions: The results of this study are adequate to demonstrate that the proposed thermal electrofogger use will not result in residues that exceed the established tolerance of 5.0 ppm for pome fruit. HED thus recommends in favor of the proposed registration of ecoFOG-80 FDL.



Primary Evaluator	 George F. Kramer, Ph.D., Senior Chemist Risk Assessment Branch 1 (RAB1) Health Effects Division (HED) (7509P)	Date: 28-JUN-2012
Approved by	 David E. Hrdy, Acting Branch Chief RAB1/HED (7509P)	Date: 28-JUN-2012

STUDY REPORT:

48630609. Mallipudi, N. (2011) Magnitude of the Residue of Fludioxonil on Pome Fruit Following Post-Harvest Application by Fogging. Lab Project Number: 31797. Unpublished study prepared by Pace International, LLC. 67 pages.

EXECUTIVE SUMMARY:

A single post-harvest trial using apples was conducted during 2011. EXC6021 (liquid end-use product; 8% fludioxonil) was applied post-harvest by thermal fogging to Red Delicious apples in a simulated controlled-atmosphere cold storage warehouse at a nominal rate of 0.0094 lb ai/ton. The untreated fruit samples were taken one day prior to application. Four treated samples were sampled at a 1-day post-treatment interval (PTI). Samples were stored frozen from collection to analysis for <1 month, an interval supported by available storage stability data.

Samples were extracted and the extract was analyzed by gas chromatography with a mass-selective detector (GC/MSD) for residues of fludioxonil. The method was adequately validated in conjunction with the analysis of treated samples and limit of quantitation (LOQ) was 0.1 ppm. Residues of fludioxonil in the control samples were <LOQ. A single application of fludioxonil (EXC 6021) resulted in maximum fludioxonil residues of 0.26-0.34 ppm (n=4) with a mean of 0.303 ± 0.038 ppm in apples sampled at a 1-day PTI.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the post-harvest residue data on apples are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 396217].

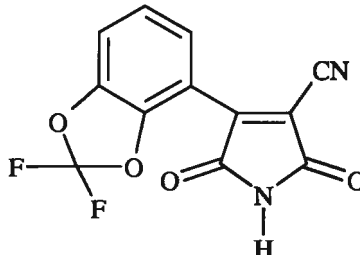
COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. None of the reported deviations affects the acceptability of the study.

**A. BACKGROUND INFORMATION**

Fludioxonil is a contact fungicide, which inhibits protein kinase, leading to reduced fungal growth and development. Tolerances are currently established for residues of fludioxonil, 4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1*H*-pyrrole-3-carbonitrile, in/on various plant commodities at levels ranging from 0.01-500 ppm [40 CFR §180.516], including a 5.0-ppm tolerance for the pome fruit crop group.

TABLE A.1. Fludioxonil Nomenclature.

Compound	
Common name	Fludioxonil
Company experimental name	CGA-173506
IUPAC name	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1 <i>H</i> -pyrrole-3-carbonitrile
CAS name	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1 <i>H</i> -pyrrole-3-carbonitrile
CAS registry number	131341-86-1
End-use products (EP)	Scholar [®] Fungicide (50% WP; EPA Reg. No. 100-969) Scholar [®] Fungicide (1.9 lb/gal SC; EPA Reg. No. 100-###)

**TABLE A.2. Physicochemical Properties of Fludioxonil.**

Parameter	Value	Reference
Melting point	199.8 °C	DP# 348539, D. Rate, 09/10/08
pH	8-9 @ 25 °C (1% aqueous dispersion)	
Density	1.54 g/cm ³ typical at 23 °C	
Water solubility (25 °C)	1.8 mg/L	
Solvent solubility (g/L at 20 °C)	Ethanol 44,000 Acetone 190,000 Toluene 2,700 n-Octanol 20,000 n-Hexane 7.8	
Vapor pressure at 25 °C	2.9 x 10 ⁻⁹ mm Hg	
Dissociation constant (pK _a)	pK _{a1} <0 pK _{a2} ~14.1	
Octanol/water partition coefficient, Log(K _{ow})	4.12 @ 25 °C	
UV/visible absorption spectrum	12,384 L/mol x cm @ 266 nm (neutral solution) 12,327 L/mol x cm @ 265 nm (acidic solution) 11,790 L/mol x cm @ 271 nm (basic solution)	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

The untreated apples used for post-harvest treatment were purchased from a local organic grower. As applications were made post-harvest at indoor facilities, variables such as soil type, length of growing season, and weather are not relevant to the current study.

The field phase of the study was conducted at Pace International LLC in a research-sized fumigation room. On the day before treatment, 24 individual open-air plastic crates were prepared for fogging by placing approximately 50 pounds of apples in each crate. In 16 crates, one mesh bag containing 6 apples was placed in the bin with other apples surrounding it. The other eight crates contained apples without a mesh bag and were used to fill excess space in the fogging chamber. To protect from direct spray of the fogger, cardboard sheets were placed over the tops and over the front surface of the stacks of crates. The apples were left in the fogging chamber overnight to acclimate to the temperature and humidity of the room. A custom-made fogging machine was used for the application of test substance to the apples. EXC6021 (liquid end-use product; 8% fludioxonil) was applied at a nominal rate of 0.0094 lb ai/ton

TABLE B.1.1. Study Use Pattern on Apples: Post-harvest Application of Fludioxonil.

Location City, State; Year (Trial ID)	Post-harvest Application				
	Formulation	Method; Timing	Single Rate (oz. ai/ton)	Total rate (oz. ai/ton)	Additives
Wapato, Washington; 2011 (S11-00831-0)	EXC6021 (a liquid formulation containing 8% ai)	Thermal Fogging	0.15	0.15	--



TABLE B.1.2. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Apple		
	Submitted	Requested	
		Canada	U.S.
Not applicable to this study. ¹			

¹ As the use pattern was a postharvest thermal fog, geographic representation is not applicable to this submission.

B.2. Sample Handling and Preparation

Five samples were collected, one control and four treated. The untreated sample was taken from the supply of apples one day prior to application. The treated samples were taken approximately 24 hours after application. Samples were collected into residue bags and placed into separate ice chests with dry ice for transport and shipment. For analysis, the prepared samples were later shipped frozen to Product Safety Labs, East Brunswick, NJ, where samples were stored at <-18 °C.

B.3. Analytical Methodology

Apple samples were analyzed using GC/MSD "SOP # 62, Fludioxonil Analysis," Dale Hanks, July 28, 2006. Samples are homogenized by blending the weighed fruit sample with an equal amount of a 60% tetrapotassium pyrophosphate solution. An aliquot (~100 g) of the resultant slurry solution is extracted with 50 mL of 75% *n*-hexane:25% methyl ethyl ketone by manually shaking for 30 seconds. The extract is centrifuged and an aliquot of the supernatant is transferred to an auto-sampler vial. The fludioxonil content of the extract is determined by GC/MSD. The LOQ is 0.1 ppm.

In conjunction with the analysis of field trial samples, the above method was validated using control samples of apples fortified with fludioxonil at 0.1 and 1.0 ppm.

C. RESULTS AND DISCUSSION

The GC/MSD used to determine fludioxonil residues in/on apples was adequately validated in conjunction with the analysis of treated samples. Concurrent method recoveries from samples fortified at 0.1 and 1.0 ppm ranged from 63-88% and the overall average was 79 ± 9.8% (Table C.1). Apparent residues of fludioxonil were <LOQ in/on all control samples. The validated method LOQ is 0.1 ppm. Adequate sample calculations and example chromatograms were provided.

Apple fruit samples were stored for <1 month prior to extraction for analysis (Table C.2). Adequate storage stability data are available indicating that fludioxonil is stable at -20 °C for up to 28 months on grapes (D258870, W. Donovan, 12/20/99). These data will support the frozen storage intervals in the current trials.

A single application of fludioxonil (EXC 6021) resulted in maximum fludioxonil residues of 0.26-0.34 ppm (n=4) with a mean of 0.303 ± 0.038 ppm in apples on the day following application.

**TABLE C.1. Summary of Concurrent Method Recoveries of Fludioxonil from Pome Fruits.**

Analyte	Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean \pm std dev (%)
Fludioxonil	Apple	0.10	3	63, 81, 73	72 \pm 9.0
		1.0	3	87, 84, 88	86 \pm 2.1
		Overall	6	63-88	79 \pm 9.8

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (months)	Interval of Demonstrated Storage Stability (months) ¹
Apples	-18	<1	28

¹ D258870, W. Donovan, 12/20/99.**TABLE C.3. Residue Data from Post-harvest Apple Trials with Fludioxonil.**

City, State; Year (Trial ID)	Crop; Variety	Formulation	TRT #	Total Rate (oz. ai/ton) ¹	Commodity	PTI ² (days)	Fludioxonil Residues (ppm) ³
Wapato, Washington; 2011 (S11-00831-0)	Apple; Red Delicious	EXC6021 (liquid formulation containing 8% ai)	1	0.15	Fruit	0	0.283, 0.329 0.340, 0.260

¹ The validated method LOQ is 0.02 ppm.**TABLE C.4. Summary of Residue Data from Post-harvest Apple Trials with Fludioxonil.**

Commodity	Method of Applic.	Total Applic. Rate (oz ai/ton)	Pyrimethanil Residue Levels (ppm)						
			n	Min.	Max.	HAFT ¹	Median	Mean	Std. Dev.
Apple, fruit	Postharvest thermofog	0.15	4	0.260	0.340	NA ¹	0.306	0.303	0.038

¹ HAFT = highest-average field trial. NA = not applicable to this submission.

D. CONCLUSION

A single post-harvest trial using apples was conducted during 2011. Fludioxonil was applied post-harvest by thermal fogging to Red Delicious apples in a simulated controlled-atmosphere cold storage warehouse at a nominal rate of 0.15 oz. ai/ton. Four treated samples were taken approximately 24 hours after application. Samples were stored frozen from collection to analysis for <1 month, an interval supported by available storage stability data.

Samples were extracted and the extract was analyzed by GC/MSD for residues of fludioxonil. A single application of fludioxonil resulted in maximum fludioxonil residues of 0.26-0.34 ppm (n=4) with a mean of 0.303 \pm 0.038 ppm in apples sampled 1-day PTI.

E. REFERENCES

DP #: 258870
Subject: PP# 7E04919. Fludioxonil for use on Grapes. Evaluation of Residue Data and Analytical Methods.
From: W. Donovan
To: M. Waller
Dated: 12/20/99



Fludioxonil/071503/Pace International, LLC
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD II A 6.3.1, 6.3.2, 6.3.3 and III A 8.3.1, 8.3.2, 8.3.3
Crop Field Trial – Pome Fruits (Post-harvest use).

F. DOCUMENT TRACKING

RDI: RAB1 Chemists (6/27/12)

Petition Number(s): NA

DP#: 396217

PC Code: 071503

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